Davies, A., Teare, L., Falder, S., Dumville, J., Shah, M., Jenkins, A. T. A., Collins, D., Dheansa, B., Coy, K., Booth, S., Moore, L., Marlow, K., Agha, R., & Young, A. (2020). Consensus demonstrates four indicators needed to standardize burn wound infection reporting across trials in a single-country study (ICon-B study). *Journal of Hospital Infection*, *106*(2), 217-225. https://doi.org/10.1016/j.jhin.2020.07.022

Title: Consensus demonstrates four indicators needed to standardise burn wound infection reporting across trials in a single country study (The ICon-B Study)

Authors: Anna Davies[1], Louise Teare[2], Sian Falder[3], Jo Dumville[4a,b], Mamta Shah[5], Toby Jenkins[6], Declan Collins[7a,b], Baljit Dheansa[8], Karen Coy[9], Simon Booth[10a,b], Luke Moore[11a,b], Karen Marlow[3], Riaz Agha[12], Amber Young[9, 13] (corresponding)

Running title: Consensus to standardise burn wound infection reporting across trials (ICon-B)

Keywords: core indicator set, burn wound infection, burns, Delphi survey, consensus

[1]Centre for Academic Child Health, University of Bristol, Bristol, UK. anna.davies@bristol.ac.uk

[2] St Andrews Centre for Plastic Surgery and Burns, Mid and South Essex NHS Foundation Trust. louise.teare@meht.nhs.uk

[3] Alder Hey Children's NHS Foundation Trust, Liverpool, L14 5AB, UK. Sian.falder@alderhey.nhs.uk, karen.marlow@alderhey.nhs.uk

[4a]Division of Nursing, Midwifery and Social Work, School of Health Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK; [b]Manchester University NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK jo.dumville@manchester.ac.uk

[5] Royal Manchester Children's Hospital MFT NHS Foundation Trust. Manchester M13 9WL UK mamta.shah@mft.nhs.uk

[6] Department of Chemistry, University of Bath, Bath, BA2 7AY, UK a.t.a.jenkins@bath.ac.uk

[7a] Department of Plastic Surgery and Burns, Chelsea and Westminster NHS Foundation Trust, London, UK; [b]Department of Cancer and Surgery, Imperial College London, UK Declan.collins@chelwest.nhs.uk

[8] Department of Plastic Surgery, Queen Victoria Hospital, Holtye Road, East Grinstead, West Sussex, RH19 3EB, UK; b.dheansa@nhs.net

[9] Children's Burns Research Centre, University Hospitals Bristol NHS Trust, Bristol, UK. karen.coy@uhbristol.nhs.net

[10a] McIndoe Burn Centre, Queen Victoria Hospital, Holtye rd., East Grinstead, RH19 3DZ, UK. ; [b] School of Pharmacy and Bimolecular science, University of Brighton, Lewes rd., Brighton BN2 4GJ; Simon.booth@nhs.net

[11a]Chelsea and Westminster NHS Foundation Trust, 369 Fulham Road, London, SW10 9NH. UK. [b]National Institute for Health Research Health Protection Research Unit in Healthcare Associated Infections and Antimicrobial Resistance, Imperial College London, Hammersmith Campus, Du Cane Road, London. W12 0NN. UK luke.moore@chelwest.nhs.uk.

[12] Bart's Health NHS Trust, London, UK; mail@riazagha.com

[13] (Corresponding) Bristol Centre for Surgical Research, Population Health Sciences, Bristol Medical School, University of Bristol, UK amber.young1@nhs.net. Address for correspondence: Bristol Centre for Surgical Research, Bristol University, Canynge Hall, Bristol, BS8 2PS

SUMMARY

Introduction: Evidence-based interventions are needed to treat burn wound infection (BWI). Evidence syntheses have been limited by heterogeneity of indicators used to report BWI across trials. Consistent reporting of BWI would be facilitated by an agreed minimum set of indicators. The Infection Consensus in Burns study aimed to achieve expert consensus about a Core Indicator Set (CIS) for BWI.

Methods: The CIS was established through development of a long-list of BWI indicators identified from a systematic review and expert input. In a Delphi survey, UK expert participants rated the indicators according to use in everyday practice, importance for diagnosis and frequency of observation in patients with BWI. Indicators were included in the CIS if $\geq$75% of participants agreed it was important for diagnosis and used in everyday practice, and $\geq$50% rated it as frequently observed in patients with BWI.

Results: 195 indicators were identified from the systematic review and reduced to 29 survey items through merging of items with the same meaning. Seventy-five UK experts participated in the Delphi survey. Following a single survey round and a consensus meeting with an expert panel, four items were included in the CIS: pyrexia, spreading erythema, change in white cell count, and presence of pathogenic microbes.

Discussion and conclusions: To facilitate evidence synthesis, a single country systematic, expert-informed approach was taken to develop a core set of indicators (CIS) to be reported consistently across trials reporting BWI as an outcome. Future work requires verification of the CIS with international experts.

INTRODUCTION

Research studies suggest that 10-20% of people with burns develop a burn wound infection (BWI).[1-3] BWI delays healing, increases risks of scarring, and sepsis if untreated. These will increase length of hospital stay, number of operative events and healthcare costs.[4, 5] In patients with burns larger than 40% total body surface area, infection has been causally associated with 75% of deaths.[2, 6] Interventions for BWI are needed to improve patient outcomes and decrease healthcare costs.

To select interventions for BWI to achieve optimal patient outcomes, evidence is needed from high-quality RCTs, aggregated in systematic reviews.[7] Evidence synthesis can be adversely impacted by varying definitions of a single outcome across trials. This heterogeneity can cause differing estimations of the effects of the same intervention across studies, and is common.[8, 9] In a review of surgical site infection, 41 differing definitions were identified across 90 studies.[10] In a review investigating oesophagectomy outcomes, 22 different definitions of anastomotic leak were reported across 28 studies[11]. Cochrane burn care reviews report that varying definitions of BWI have prevented accurate assessment of intervention effectiveness across trials.[12, 13] In a systematic review of BWI definitions, 27 different indicators of BWI were reported across 41 studies.[14]

One reason for this heterogeneity is the lack of an objective reference standard for clinical diagnosis of BWI. Diagnosis is based on clinician judgement, informed by indicators of BWI, comprising patient-reported symptoms, clinician-observed signs and non-specific laboratory tests to detect systemic inflammation, as well as presence of bacteria in the wound. However, presence of bacteria in the wound is correlated with, but not diagnostic of, clinical infection and may simply represent wound colonisation.[15, 16] To address this difficulty with BWI diagnosis, consensus criteria have been developed from the American Burn Association (ABA)[17], Centre for Disease Control (CDC)[18], and European Wound Management Association(EWMA)[19]. However, these criteria are infrequently used in research and have clinical limitations.[14] Numerous indicators are included in these criteria, which complicates diagnosis and reporting. There is also the mandated use of wound biopsies in ABA and CDC criteria.[17, 18] Wound biopsy is invasive, increases risk of infection and scarring[20], and is not used in all countries. Wound swabs are the primary means to determine presence of bacteria in the wound.[21] The EWMA consensus criteria[19] prioritise use of indicators that are rarely seen (e.g. Ecthyma Gangrenosum). Furthermore, the EWMA consensus criteria do not include patient-reported symptoms of BWI.

To achieve consistent reporting of BWI across trials, consensus is needed about a minimum set of the most important clinical indicators to be reported; a Core Indictor Set (CIS). We define *most*

important as important to BWI diagnosis, frequently observed in patients, and commonly used to diagnose BWI in clinical practice. To ensure relevance and uptake by researchers, the selected indicators should address the above-described limitations of the described consensus criteria. A CIS will provide a minimum dataset to standardise reporting about BWI in trials reporting this outcome without limiting the reporting of other indictors. This will reduce clinical heterogeneity between studies, facilitating more efficient evidence synthesis, and enabling faster identification of effective treatments for patients.

The aim of the Infection Consensus in Burns Study (ICon-B), is to agree a CIS for BWI. The ICon-B study represents the first stage, undertaken in the UK, of an international effort to agree a CIS.

METHOD

The objectives of the ICon-B study are to:

- Establish a long-list of candidate clinical indicators for reporting BWI (Stage 1).
- Conduct a Delphi survey with UK BWI experts to achieve consensus in indicator prioritisation (Stage 2).
- Select the final CIS for reporting BWI based on the results of the Delphi survey and agreement between the ICon-B expert panel (Stage 3).

Protocol: The protocol for this study was registered on the PROSPERO database and is published (Reference CRD42018096647).[22] Changes to this protocol are justified in this paper.

Scope: The CIS will be applicable to reporting BWI outcomes in clinical trials involving patients of any age with acute (before healing) burn wounds of any size and aetiology, in in- and out-patient settings. It is not designed for use in trials reporting sepsis secondary to burns.

Study expert panel: The panel comprised 14 health care professionals (HCPs) and researchers expert in BWI, including burn surgeons (BD, DC, SF, MS, RA), clinical microbiologists (LT, LM), academics in burn research (AD, AY, JD), burns research nurses (KC, SB, KM), and a biochemist (ATAJ).

Patient and public involvement: Patients were not involved in this first stage study. While patients can report symptoms of BWI, they are not involved in interpreting clinician-observed signs and tests. Therefore, it would be unreasonable to expect patients to prioritise BWI indicators in a Delphi survey. Patients will be involved in a future international study to support clarification of definitions of patient-reported symptoms of BWI, where applicable.

Stage 1: Establishing the long list of BWI candidate clinical indicators

We define clinical indicators as:

- Patient-reported symptoms (e.g. change in wound appearance, increased pain).
- Clinician-observed signs (e.g. spreading erythema, pyrexia, purulent exudate).
- Laboratory tests for systemic inflammation (e.g. white blood cell count, C-Reactive Protein) and the presence of microbes in the wound (bacteria from wound swab or biopsy).

Systematic review (SR):

Candidate clinical indicators for the Delphi survey were identified from a systematic review of randomised controlled trials and observational studies of interventions reporting a BWI outcome.[14] An electronic search of four databases (Ovid MEDLINE, Ovid Embase, Cinahl, Cochrane Register of Trials) was conducted. Inclusion criteria were:

- Published January 2010-November 2016
- Full-text article
- Reporting an observational study or randomised controlled trial
- Reporting data on acute burn wound injuries.
- Written in English.
- Carried out in a clinical setting.
- Reporting BWI as an outcome and not wound colonisation alone.
- A human study.

Additional consensus criteria/ BWI definitions: The study expert panel were asked to identify additional articles describing indicators to define BWI.

Screening: Identified studies were systematically screened using the inclusion criteria, in two stages (abstract, title and then full text) by one researcher, with a second researcher screening 20% of studies. Disagreements were resolved via discussion, with a third reviewer where needed.

Data extraction: The indicators used to define BWI were extracted verbatim from studies. Where consensus criteria or another author's definition of BWI was cited, we accessed the primary study and extracted the indicators directly. The following data were recorded in a MS Excel spreadsheet:

- Study identifiers (author name, date of publication).
- Indicators used to define BWI, extracted verbatim from methods/ results.
- Whether the indicator was reported in a primary study or derived from a consensus statement.

Identifying unique indicators to inform survey items:

Following extraction, one researcher (AD) carried out preliminary de-duplication, sorting indicators with the same/similar meaning into groups where the similar terminology had been used (e.g. '*presence of microbes'* and '*presence of pathogens*' in the wound). Similar indicators using differing terminology, or that were unclear in their meaning, were organised as separate groupings for review (e.g. '*rapid associated change in burn wound appearance or character',* and '*unfavourable and unexpected local evolution'*).

The expert panel met to review the long list and to confirm or reject the decisions about potential duplicates and potentially redundant indicators (e.g. those relating to sepsis only). A unique definition of each indicator was agreed through iterative discussion.

Stage 2: Delphi Survey of infection indicators

The Delphi technique was selected to gather data from a range of stakeholders.[23] A Delphi survey to achieve expert consensus is recommended by the Core Outcome Measures in Effectiveness Trials (COMET) group for development of Core Outcome Sets (COS)[24]. Delphi surveys have been successfully used to develop criteria for a clinical diagnostic tool for hepatic and renal cyst infection [25] and for diagnosis of paediatric joint or bone infection[26]. Delphi surveys use iterative questionnaire rounds, between which data are summarised. The responses are anonymously fed back to stakeholders within any subsequent rounds to enable consensus. The anonymity of Delphi surveys may facilitate gathering of more truthful views from respondents,[27] and can be administered electronically to gather opinions of a larger number of stakeholders than can be achieved face-to-face.

Ethics

No ethical approval for the Delphi survey was required, as the research was conducted outside the NHS.

Delphi sample size

There are no guidelines to determine the number of participants needed for a Delphi Survey. The COMET handbook recommends representation from each stakeholder group to enable

generalisation of findings[24]. We aimed to achieve representation from multi-disciplinary BWI experts from all four UK countries and as many burns services as possible.

Participants

Stakeholders were invited to take part if they were UK-based HCPs in burn care and diagnosis of BWI from the following groups:

- Consultant plastic/burn surgeons.
- Trainee plastic surgeons with at least three consecutive months' burn care experience.
- Burn care and research nurses with at least three consecutive months' burn care experience.
- Clinical microbiologists involved in BWI diagnosis, working in a hospital with a burns service.
- General practitioners who had seen at least one suspected BWI in the preceding month.
- Emergency department staff who had seen at least one suspected BWI in the preceding month.
- Intensivists/anaesthetists working in burn care.

Participants were approached by email through professional organisations: British Burn Association (BBA), Care of Burns in Scotland (COBIS), the Faculty of Intensive Care Medicine and the National Academic Mailing List service (JISC Burns Research). Twitter and personalised emails to contacts of the expert panel in all four UK countries were used.

Survey items

The Delphi survey comprised demographics questions and BWI indicator items:

i. Demographic questions:

- *Job role,*
- Patient group worked with (adults, children, both).
- UK country and burns service.

ii. BWI indicators:

Each candidate clinical indicator, referred to as a survey 'item' was assigned to patient-reported symptoms, clinical signs or laboratory tests. For each item, three questions were asked with the following response scales:

1. *Do you routinely use this indicator to diagnose burn wound infection in your day to day practice?*

Participants recorded their response by selecting 'yes' or 'no'.

2. How important is this indicator in diagnosing burn wound infection in your everyday practice?

Participants recorded their response on a Likert-type scale with text anchors, ranging from 1 to 9, where 1-3 indicated 'not at all important', 4-6 indicated 'important but not vital' and 7-9 indicated 'very important'.

2. How frequently do you see this symptom/sign in patients you diagnose with burn wound infection?

Participants recorded their response on a Likert-type scale with text anchors, ranging from 1 to 9, where 1 indicated 'very infrequently' and 9 indicated 'very frequently'.

For each question participants could state they did not have an opinion about the indicator (0).

Survey piloting:

The survey was piloted in the UH Bristol NHS Foundation Trust burns service, emergency department and clinical microbiology team. Participants recorded whether they understood the survey purpose, the completion instructions, whether questions were unclear, and if they had additional indicators to include. Feedback revealed that some participants had misunderstood the survey purpose; that they believed it aimed to develop a diagnostic tool. This informed the participant information at the start of the survey.

Following piloting, an online survey was developed in REDCap (Research Electronic Data Capture [28, 29]. The survey URL was distributed by email, using the mailing lists and of the above described organisations and the expert panel's contacts.

Data extraction and analysis:

Any individual who completed the consent form, provided their email address, and provided a response to at least one survey item, was considered a survey participant. Any completed datapoint was included in the dataset to maximise data available for analysis. For each item, descriptive data were produced:

- Number of participants completing the item.

- Number and percentage of participants indicating '0' (no opinion).
- Number and percentage of participants rating the items 'yes' and 'no', where applicable (question 1), and 1-3, 4-6 or 7-9 for the Likert-type scales (questions 2 and 3).

Data were tabulated for each item, excluding 0 responses (no opinion). Percentages for the number of participants rating the item as 'yes' or 'no' (question 1), and 1-3, 4-6 and 7-9 (questions 2 & 3) were calculated with the denominator being the number of participants who completed the item with a value above 0 (no opinion) i.e. 1-9, or yes/no.

Dropping and modification of items between survey rounds: The threshold for items to be carried through to the second round and expert panel meeting were pre-specified.[22] Items were carried through to a second round of the survey if ≥75% of participants stated that they used the indicator to diagnose BWI as part of their everyday practice (question 1). If so, the item would be included in the next round if: ≥75% of participants rated it as 7-9 on the importance scale *and* 7-9 on the frequency scale, with ≤15% rating it as unimportant/infrequently seen (1-3) on either scale.

Stage 3: Consensus meeting with ICon-B expert panel

After completion of the survey first round, the expert panel met to review the survey data and identify next steps.

RESULTS

Stage 1: Establishing a long list of BWI candidate indicators

Systematic review

Of 2,056 identified studies, 72 met the inclusion criteria. Of these, 44 described the indicators used to define BWI (see figure I).

Six studies cited the use of a set of consensus criteria (ABA)[17], and two cited the use of another author's definition of BWI.[30, 31] The expert panel recommended the inclusion of the EWMA[19] and CDC[18] consensus criteria.

Identifying unique indicators to inform survey items

From the 44 studies, the three sets of consensus criteria and the two cited BWI definitions, 195 BWI indicators were extracted. Following initial de-duplication and grouping of the indicators undertaken by one researcher (AD), 75 groups of indicators were presented to the expert panel. These were iteratively reviewed for duplication and redundancy, resulting in 27 unique indicator items for the survey (Appendix A). Two additional items were added, as one indicator could be both patient-reported and clinically observed (wound smell), and one indicator comprised two items (colour and volume of exudate).

Stage 2: Delphi survey

Demographic characteristics of participants

Ninety-six participants viewed the survey, of which 75 (78%) completed at least one indicator item. The demographic characteristics of the participants are presented in table I.

Ratings of BWI clinical indicators

1. *Use of the indicator in everyday practice*

Table II indicates participant ratings for the 29 survey items.

Nine items met the pre-specified threshold for use of the indicator in everyday practice ($\geq$75% of participants indicating yes): high temperature, spreading erythema, clinician-observed wound smell, change in colour of exudate, wound or surrounding skin hot, change in C-Reactive Protein, change in white blood cell count, bacteria in blood, and potentially pathogenic microbes identified from wound swab.

2. *Importance of the indicator for diagnosing BWI*

Eight items met the pre-specified threshold for being very important (rated 7-9) for diagnosis of BWI by $\geq$75% of participants (Table II, second column). Three items were viewed as important for diagnosing BWI but were not used by $\geq$75% of participants in everyday practice for diagnosis. These were ascending lymphangitis, (no) signs of alternative infection, and invasion of bacteria through biopsy/tissue culture. Five items met the threshold for use of the indicator in everyday practice: high temperature, spreading erythema, change in white blood cell count, bacteria in the blood, potentially pathogenic microbes from wound swab

3. *Frequency with which indicators are seen in patients diagnosed with BWI*

No indicators met the pre-specified threshold for frequency of observation in patients diagnosed with BWI.

Stage 3: Consensus meeting with ICon-B expert panel

Following discussion, the expert panel agreed a variation to the study protocol. They agreed to reduce the threshold for carrying items through where ≥ 50% of participants had rated that they observed the indicator very frequently (7-9) in patients with BWI.

Eight indicators met this threshold: high temperature, change in C-Reactive Protein, change in white blood cell count, potentially pathogenic microbes from wound swab, patient feels unwell, spreading erythema, improvement in the patient's condition following administration of antimicrobials, and wound smell. Of these, only four also met the ≥75% threshold for use of the indicator in everyday practice, and importance of the indicator for diagnosing BWI. These were: high temperature, spreading erythema, white cell count, and potentially pathogenic microbes from the wound swab.

In a further protocol variation, the expert panel agreed that a second round of the survey was not necessary in this stage one study. Applying the thresholds described above, there was consensus about only four items. These were:

- Pyrexia
- Spreading redness in unburned surrounding tissue (spreading erythema)
- Change in white blood cell count (leucocytosis)
- Presence of potentially pathogenic microbes identified from burn wound swab

DISCUSSION

The use of varying indicators to define BWI has hindered accurate conclusions being drawn about intervention effectiveness in Cochrane reviews.[12, 13] The aim of the ICon-B study was to agree a core set of the most important indicators of BWI, to support consistent reporting across clinical burn care trials and more effective evidence synthesis. *Most important* was defined as the indicator being a priority for diagnosis, used in everyday clinical practice and frequently seen in patients with BWI. Consensus was achieved for four clinical indicators: pyrexia, spreading erythema, change in white blood cell count, and potentially pathogenic microbes present in the wound (identified from wound swab). The CIS provides a minimum dataset to be reported across trials for BWI while allowing the reporting of other indictors relevant to the research question. It does not represent a definition of BWI or a clinical tool for diagnosis. The approach taken in this study is similar to that used by researchers who aimed to identify clinical indicators for biofilm and local infection in chronic wounds

of all types.[32] The expert consensus methodology that we have used could be replicated to identify other core indicators to be reported for other outcomes for which no accepted standard is available. In burn care this may include wound healing, quality of life, or scarring, which are all multidimensional and informed by several indicators.[33-35]

Previous consensus-informed standards to address heterogeneity in the indicators used to report BWI have not been adopted in routine practice or for research.[17-19] This is due to limitations including the use of indicators that are not used to diagnose BWI in all patients, or in all countries (e.g. wound biopsy[17, 18]), and the incorporation of indicators rarely seen in patients with BWI (e.g. Ecthyma Gangrenosum[19]). We have addressed these by identifying indicators used in everyday practice and frequently seen in patients diagnosed with BWI. This will ensure that data collection can be undertaken as part of usual care. An unexpected finding was that no indicator was reported by at least 75% of participants as frequently observed in patients with BWI. This highlights the multiple signs and symptoms used in its clinical diagnosis. Through agreement with the expert panel, a pragmatic approach was taken; the threshold for use in the CIS was agreed to be more than 50% of participants reporting that the indicator is seen frequently in patients with BWI.

The strengths of this study are that we used a pre-defined protocol to identify the CIS and achieved representation from many disciplines involved in the diagnosis and treatment of patients with BWI. We have transparently reported two changes to the protocol. We achieved representation of participants from three of the four UK countries. Expansion to an international audience will be important, to ensure relevance and acceptability of the CIS to global researchers. It is possible that HCPs working in low resource settings may have differing views about which indicators are most important and differing resources available to conduct relevant tests. This issue can be addressed by asking global researchers whether indicators are used to inform diagnosis in daily practice.

Limitations of this study are that only one Delphi survey round was conducted. This decision was reached through expert panel agreement that consensus had been achieved for four indicators within one round. We acknowledge that Delphi surveys typically involve more than one round, to enable feedback of participants' responses to reach consensus. We anticipate that extending this survey to an international audience, where there may be greater variation in practices, will require a survey with two or more rounds to achieve consensus.

Our study has identified a core set of indicators considered most important for reporting BWI outcomes with experts from UK burn services. If adopted by investigators, the CIS will improve the consistency with which BWI is reported across trials. This will reduce clinical heterogeneity and facilitate efficient and valid evidence syntheses. Further work is needed to agree the CIS

internationally. Other work will be undertaken to define metrics for the final chosen indicators. Two of the four CIS indicators (pyrexia and white cell count) are reported as numerical values. The presence of potentially pathogenic microbes is usually assessed quantitatively and/or qualitatively, and erythema is a clinical judgement.

Conclusions: This study has taken a systematic approach to agreeing the most important indicators for reporting BWI consistently across trials. We have called this a CIS. If implemented, this CIS will reduce clinical heterogeneity between trials and support efficient evidence synthesis, to identify the most effective treatments and inform clinical decision-making for patients with burn injuries. Further work will be required to verify the CIS with international professionals and patients.

Author contributions: AY and AD devised the project along with ATAJ. AD and AY developed the protocol and AD collected and analysed the data. LT, SF, JD, MS, DC, BD, KC, SB, LM, KM, and RA provided clinical burns and microbiology expertise, attended steering meetings, participated in the expert panel and supported recruitment to the study. All authors read and provided input to each draft of the paper.

Acknowledgements: We are grateful for the responses from all colleagues who participated in the Delphi survey across the UK. We thank Rob Maybin, and colleagues at United Hospitals Bristol NHS Trust for their contributions to the survey pilot.

Declaration: All authors have reviewed and approved the final article.

Conflict of interest statement: LM has consulted for DNA electronics (2015-18), Dairy Crest (2017–2018), Umovis Lab (2020), received speaker fees from Profile Pharma (2018) and Pfizer (2018-2020), received research grants from the National Institute for Health Research (2013-2020), CW+ Charity (2018-2020), and Leo Pharma (2016), and received educational support from Eumedica (2016–2018).

The other authors report no conflicts of interest.

Funding source: This study was funded by an MRC grant (MR/N006496/1) and EPSRC grants (EP/R51164X/1 and EP/R003939/1).

LM acknowledges support from the National Institute of Health Research (NIHR) Imperial Biomedical Research Centre (BRC) and the National Institute for Health Research Health Protection Research Unit (HPRU) in Healthcare Associated Infection and Antimicrobial Resistance at Imperial College London in partnership with Public Health England. The views expressed in this publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research, or the UK Department of Health.

REFERENCES

[1] Church D, Elsayed S, Reid O, Winston B, Lindsay R. Burn Wound Infections. Clinical Microbiology Reviews. 2006;19(2):403-34.
[2] Rafla K, Tredget EE. Infection control in the burn unit. Burns. 2011;37(1):5-15.
[3] Ravat F, Le-Floch R, Vinsonneau C, Ainaud P, Bertin-Maghit M, Carsin H, et al. Antibiotics and the burn patient. Burns. 2011;37(1):16-26.
[4] Singer AJ, McClain SA. Persistent wound infection delays epidermal maturation and increases scarring in thermal burns. Wound Repair Regen. 2002;10(6):372-7.
[5] Posluszny JA, Conrad P, Halerz M, Shankar R, Gamelli RL. Surgical Burn Wound Infections and Their Clinical Implications. J Burn Care Res. 2011;32(2):324-33.
[6] Greenhalgh DG, Saffle JR, Holmes JH, Gamelli RL, Palmieri TL, Horton JW, et al. American burn association consensus conference to define sepsis and infection in burns. Journal of Burn Care and Research. 2007;28(6):776-90.
[7] Evans D. Hierarchy of evidence: a framework for ranking evidence evaluating healthcare interventions. J Clin Nurs. 2003;12(1):77-84.
[8] Aromataris EM, Z. . Joanna Briggs Institute Reviewer's Manual: The Joanna Briggs Institute; [updated 2017. Available from: https://reviewersmanual.joannabriggs.org/.
[9] Deeks JJ, Higgins JPT, Altman DG, on behalf of the Cochrane Statistical Methods G. 2019.
[10] Bruce J, Russell EM, Mollison J, Krukowski ZH. The quality of measurement of surgical wound infection as the basis for monitoring: a systematic review. Journal of Hospital Infection. 2001;49(2):99-108.
[11] Blencowe NS, Strong S, McNair AGK, Brookes ST, Crosby T, Griffin SM, et al. Reporting of Short-Term Clinical Outcomes After Esophagectomy: A Systematic Review. Annals of Surgery. 2012;255(4):658-66.
[12] Wasiak J, Cleland H, Campbell F, Spinks A. Dressings for superficial and partial thickness burns. Cochrane Database of Systematic Reviews. 2013;2013 (3) (no pagination)(CD002106).
[13] Barajas-Nava LA, Lopez-Alcalde J, Roque i Figuls M, Sola I, Bonfill Cosp X. Antibiotic prophylaxis for preventing burn wound infection. Cochrane Database Syst Rev. 2013(6):CD008738.
[14] Davies AS-J, Francesca; Jenkins, A Toby A; Young, Amber E. A systematic review of intervention studies demonstrates the need to develop a minimum set of indicators to report the presence of burn wound infection. *in press*. Burns. 2020.
[15] Halstead FD, Lee KC, Kwei J, Dretzke J, Oppenheim BA, Moiemen NS. A systematic review of quantitative burn wound microbiology in the management of burns patients. Burns. 2018;44(1):39-56.
[16] Kallstrom G. Are Quantitative Bacterial Wound Cultures Useful? Journal of Clinical Microbiology. 2014;52(8):2753-6.
[17] Greenhalgh DG, Saffle JR, Holmes JHt, Gamelli RL, Palmieri TL, Horton JW, et al. American Burn Association consensus conference to define sepsis and infection in burns. J Burn Care Res. 2007;28(6):776-90.
[18] Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control. 2008;36(5):309-32.
[19] Cutting K.F. WRJ, Mahoney P., Harding K.G. Clinical identification of wound infection: a Delphi approach. EWMA Position document: Identifying criteria for wound infection [Internet]. 2005 17/07/2018:[6-9 pp.]. Available from: http://old.ewma.org/fileadmin/user_upload/EWMA/pdf/Position_Documents/2005__Wound_Infection_/English_pos_doc_final.pdf.
[20] Abhishek K, Khunger N. Complications of skin biopsy. J Cutan Aesthet Surg. 2015;8(4):239-41.

[21] Davies A, Spickett-Jones F, Brock P, Coy K, Young A. Variations in guideline use and practice relating to diagnosis and management of infection in paediatric burns services in England and Wales: A national survey. Burns. 2017;43(1):215-22.
[22] Davies A, Teare L, Falder S, Coy K, Dumville JC, Collins D, et al. Protocol for the development of a core indicator set for reporting burn wound infection in trials: ICon-B study. BMJ Open. 2019;9(5):e026056.
[23] Dalkey NH, O. An experimental application of the Delphi method to the use of experts. Management Science. 1963;9:458-67.
[24] Williamson PR, Altman DG, Bagley H, Barnes KL, Blazeby JM, Brookes ST, et al. The COMET Handbook: version 1.0. Trials. 2017;18(3):280.
[25] Lantinga MA, Darding AJM, de Sévaux RGL, Alam A, Bleeker-Rovers CP, Bobot M, et al. International Multi-Specialty Delphi Survey: Identification of Diagnostic Criteria for Hepatic and Renal Cyst Infection. Nephron. 2016;134(4):205-14.
[26] Mitha A, Boulyana M, Hue V, Pruvost I, Martinot A, group tEF-se, et al. Consensus in diagnostic definitions for bone or joint infections in children by a Delphi method with European French-speaking experts. Acta Paediatrica. 2012;101(8):e350-e6.
[27] Hsu C-CS, B.A. The Delphi technique: making sense of consensus. Practical Assessment, Research, and Evaluation. 2007;12.
[28] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. Journal of Biomedical Informatics. 2009;42(2):377-81.
[29] Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: Building an international community of software platform partners. Journal of Biomedical Informatics. 2019;95:103208.
[30] Peck MD, Weber J, McManus A, Sheridan R, Heimbach D. Surveillance of Burn Wound Infections: A Proposal for Definitions. The Journal of Burn Care & Rehabilitation. 1998;19(5):386-9.
[31] Silla RC, Fong J, Wright J, Wood F. Infection in acute burn wounds following the Bali bombings: A comparative prospective audit. Burns. 2006;32(2):139-44.
[32] Haesler E, Swanson T, Ousey K, Carville K. Clinical indicators of wound infection and biofilm: reaching international consensus. Journal of Wound Care. 2019;28(Sup3b):s4-s12.
[33] Lee KC, Dretzke J, Grover L, Logan A, Moiemen N. A systematic review of objective burn scar measurements. Burns Trauma. 2016;4:14-.
[34] Spronk I, Legemate C, Oen I, van Loey N, Polinder S, van Baar M. Health related quality of life in adults after burn injuries: A systematic review. PLoS One. 2018;13(5):e0197507-e.
[35] Singer AJ, Boyce ST. Burn Wound Healing and Tissue Engineering. Journal of burn care & research : official publication of the American Burn Association. 2017;38(3):e605-e13.

Figure 1: Flow diagram of process of survey item development

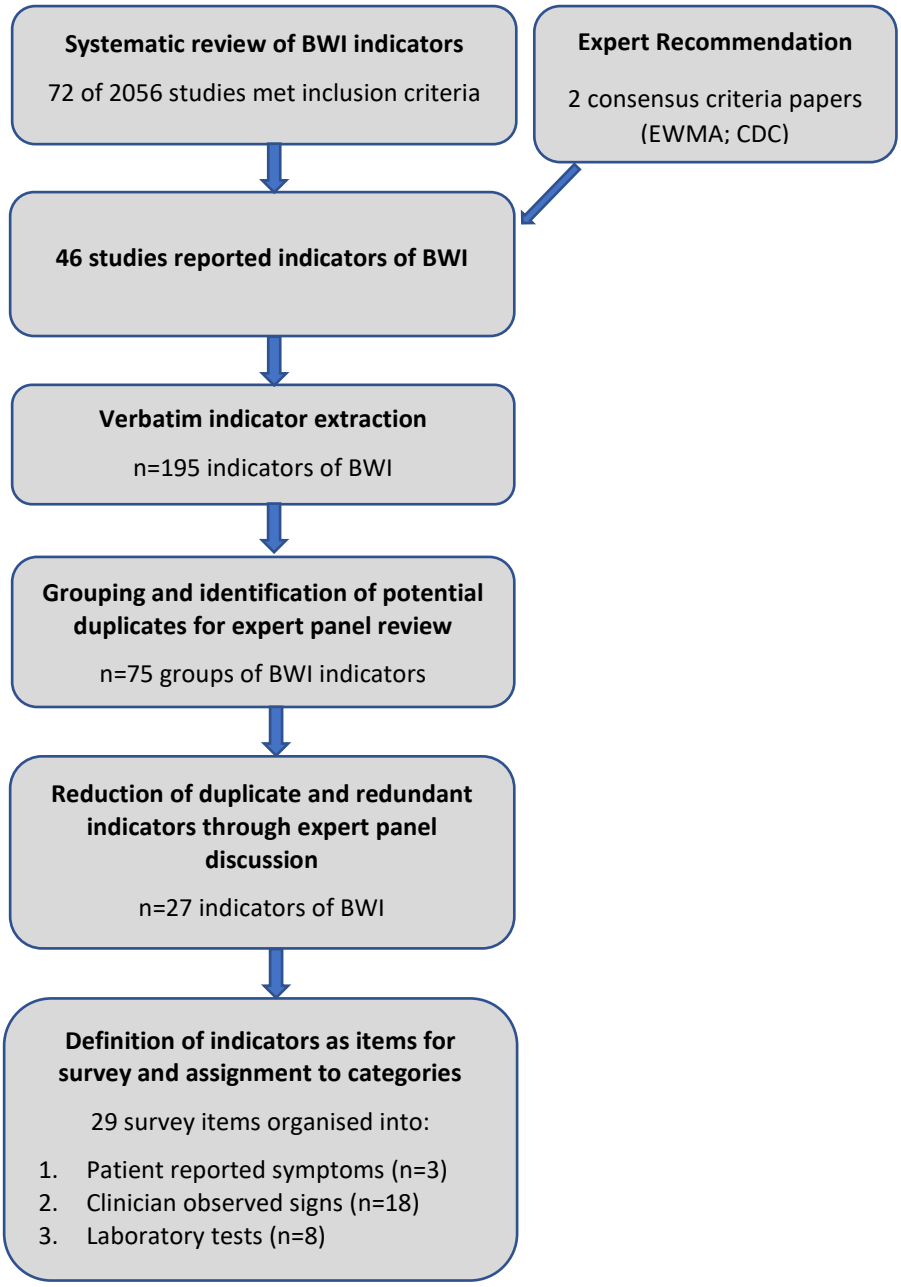

Table I: Participant demographic characteristics

Participant type	**N (%)**
Consultant plastic surgeon	9 (12)
Plastic surgery trainee	2 (2.7)
Clinical burns nurse	31 (41.3)
Burns research nurse	5 (6.7)
Clinical microbiologist / infectious diseases physician	4 (5.3)
Emergency department doctor	5 (6.7)
GP	1 (1.3)
Intensive care doctor/ anaesthetist caring for patients	8 (10.7)
Intensive care nurse caring for patients with burns	3 (4.0)
Clinical research fellow	1 (1.3)
Burns care advisor	1 (1.3)
Burns clinic coordinator	1 (1.3)
Burn ward matron	1 (1.3)
Emergency burns assessment centre nurse	1 (1.3)
Allied Health Professionals (OT, Physio)	2 (2.7)
Country	
England	62 (82.7)
Wales	8 (10.7)
Scotland	4 (5.3)
Northern Ireland	0
USA*	1 (1.3)
Patients worked with	
Adults only (≥16 years of age)	23 (30.7)
Children only (<16 years)	17 (22.7)
Adults and children	35 (46.7)

*****One USA expert completed the survey. We agreed to include their data.

Table II: Item ratings for the first round of the Delphi survey

Grey boxes indicate items reaching the inclusion threshold; bold items are those included in the CIS.

Indicator	**Participants stating YES to use of indicator in everyday practice**	**Participants rating very important (7-9) for Importance of Indicator in diagnosis of BWI**	**Participants rating very frequently (7-9) for frequency with which the indicator is observed in patients diagnosed with BWI**
	% (n)	**% (n)**	**% (n)**
Patient reported symptoms			
Patient feels unwell	74.6 (50)	65.3 (49)	53.5 (23)
Wound pain	66.1 (41)	54.8 (40)	29.6 (21)
Wound smell	65.1 (41)	47.3 (35)	36.1 (26)
Clinician observed signs			
High temperature	**87.3 (55)**	**81.2 (56)**	**70.6 (48)**
Low temperature	34.9 (22)	34.8(24)	2.9 (2)
Low blood pressure	38.1 (24)	41.2 (28)	27.5 (19)
Tachycardia	68.8 (44)	60.0 (42)	49.3 (34)
Spreading erythema	**91.2 (62)**	**88.6 (62)**	**58.0 (40)**
Ascending lymphangitis	72.3 (47)	82.1 (55)	25.8 (17)
Improvement following use of antimicrobials	62.1 (36)	59.1 (39)	51.6 (33)
Signs of alternative infection	67.2 (39)	76.1 (51)	38.5 (25)
Unexpected increase in burn depth	61.4 (35)	62.9 (39)	25.8 (16)
Unexpected change in wound colour	49.2 (30)	42.2 (27)	20.3 (13)
Wound smell	80.6 (50)	69.2 (45)	51.6 (33)
(Change in) colour of exudate	75.0 (45)	62.7 (42)	43.1 (28)
(Change in) volume of exudate	41.7 (25)	31.3 (20)	16.1 (10)
Wound or surrounding skin hot	78.1 (50)	74.2 (49)	44.4 (28)
Wound hardness	29.8 (17)	27.4 (17)	6.6 (4)
Oedema	62.9 (39)	49.2 (32)	30.2 (19)
Loss of skin graft/allograft	55.7 (34)	63.5 (40	27.9 (17)
Loss of skin substitute	65.4 (34)	69.0 (40)	26.8 (15)
Laboratory tests			
Change in C-Reactive Protein	79.3 (46)	72.1 (44)	60.0 (36)
Change in Procalcitonin	12.1 (4)	28.0 (7)	4.8 (1)
Change in blood glucose	53.5 (23)	53.1 (26)	41.7 (20)
Change in white blood cell count	**80.4 (41)**	**76.4 (42)**	**68.5 (37)**
Bacteria in blood	80.4 (41)	79.2 (42)	23.1 (12)
Invasion of bacteria through biopsy/tissue culture	68.0 (34)	83.0 (39)	32.5 (13)
Microbes from wound swab	68.0 (24)	40.7 (24)	55.2 (32)
Potentially pathogenic microbes from wound swab	**89.8 (53)**	**81.7 (49)**	**63.3 (38)**

FIGURE TITLES:

Figure 1: Flow diagram of process of survey item development